PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PRD2106f-PCT	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2004/052104	International filing date *(day/month/year)* 09.09.2004	Priority date *(day/month/year)* 10.09.2003
International Patent Classification (IPC) or national classification and IPC A61K9/00		
Applicant JANSSEN PHARMACEUTICA N.V. et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06.07.2005	15.02.2006
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Epskamp, S Telephone No. +31 70 340-

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/052104

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-70 as originally filed

Claims, Numbers

1-9 as originally filed

Drawings, Sheets

1/2, 2/2 as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2,3,5,6,9
	No:	Claims	1,4,7,8
Inventive step (IS)	Yes:	Claims	9
	No:	Claims	1-8
Industrial applicability (IA)	Yes:	Claims	1-9
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document/s/:
D1: BASF ExAct No. 5 (2000), p. 6-7: Kollidon® VA 64: An excellent dry binder. Retrieved from the Internet on 29/9/2005, http://www.pharma-solutions.basf.com/(mck0o54541nxg555xxqywy45)/pdf/ExAct/kollidon_va_64/09007ac78000e871.pdf
D2: US 6,318,650 B

Clarity

1 - The term "platelets" as used in claims 1 and 4 is vague and unclear, and does not allow the reader to define the scope of protection sought (Art 6 PCT). The definition on page 12, lines 12-14, makes clear that according to the applicant any particle with a thickness smaller than its length and width is considered a platelet. It would appear that any particle which is not a perfect sphere or cube would fall under such a definition.
2 - Claims 1-4 further lack clarity, as the polymers referred to therein are not adequately defined (Art 6 PCT).
In claims 1, 2 and 4, a polymer PVP-VA-60 is referred to. However, no such polymer appears to exist (compare the description, page 11, lines 5-6). Given the description it was assumed that PVP-VA 64 was meant.
In claims 1, 3 and 4, Eudragit-E100-PO is referred to. The use of a trademark in the claims leads to a lack of clarity, as it may not be guaranteed that the product referred to is not modified while maintaining its name during the term of the patent. Furthermore, documentation of the manufacturer only appears to refer to either Eudragit E100 (available as granules), or Eudragit E PO (powder), not to Eudragit-E100-PO. In any case, using the tradename as is done in the claims could also be seen as contradicting the fact that the particles should be shaped as platelets, since the tradename already implies a physical form (granules or powder).

Novelty

3 - Furthermore, the above-mentioned lack of clarity notwithstanding, the subject-matter of claims 1, 4, 7 and 8 is not new in the sense of Article 33(2) PCT, and therefore the criteria of Article 33(1) PCT are not met.
4 - Document D1 (page 6, middle column, par. 4; figure 2) shows that particles of Kollidon

VA 64 (PVP VA 64) have a "shell like structure". Indeed, the shape of at least some of the particles shown in figure 2 is such, that the term "platelets" is not sufficiently well-defined to distinguish the particles of claim 1 from these particles (see point 1 above).
Consequently, claim 1 lacks novelty over D1.
5 - Document D2 (column 1, lines 43-59; examples; figure 1; claims) discloses a process for producing solid particulate preparations in which a bioactive substance is homogeneously dispersed in a matrix of thermoplastic excipients. The particles are prepared in a screw extruder by melting the excipients and mixing them with the active substance, followed by cooling the mixture and grinding it to a powder in a cooling zone of the extruder. In examples 4, 7 and 9, Kollidon VA 64 is used as excipient, the use of acrylic polymers is also foreseen (column 6, lines 57-58; example 8). Given the process, at least some of the particles will have a shape which would fall under the definition for platelets given in the application (see point 1 above).
Thus, claims 4, 7 and 8 are considered to lack novelty over D2.
6 - Claims 2, 3, 5, 6 and 9, as far as clear, are considered novel.

Inventive Step

7 - Lacking novelty, claims 1, 4, 7 and 8 cannot be considered inventive (Art 33(3) PCT).
8 - Document D2 (see point 5 above) is the closest state of the art for the subject-matter of claim 9.
Claim 9 differs from D2, in that a pressurized gas is injected into the barrel of the melt extruder, followed by mixing and expanding the mixture of PVP-VA 60 or Eudragit E100 PO, (active ingredient) and gas. Furthermore a melt seal is created before the site of the gas injection.
The problem to be solved by claim 9 in view of D2 is to provide a process for forming particles, the particles having improved compressibility and being easier to mill.
Claim 9 is considered inventive (Art 33(3) PCT). Document D2 already foresees adding a (gaseous) blowing agent to the molten polymer/drug mixture, which leads to foam formation in the cooling zone of the extruder, and to more efficient comminution there (column 3, lines 23-37; column 8, line 31). However, following this suggestion of D2 indeed leads to the more comminuted particles, not necessarily to the particles resulting from the process of claim 9 which are easier to mill (in other words: which still can be milled further) and have a better compressibility. So the skilled person would not apply the suggestion to add a (gaseous) blowing agent to a molten mixture of PVP-VA 64 or acrylic polymer and

drug, to make particles which have a better compressibility and are easier to mill, as compared to the process without the addition of gas.

9 - Dependent claims 2, 3, 5 and 6 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, involve an inventive step with respect to the prior art named in the present proceedings. The reasons therefor are that the additional features of the said dependent claims are either directly known from document D2, or are a combination of features obvious to the skilled person in consideration of documents D1-D2, or they concern minor modifications which lie within the normal practice of the skilled person and/or for which nu (unexpected) technical effect has been shown.

Industrial applicability

10 - Claims 1-9 fulfill the requirements of Article 33(4) PCT.